

What is claimed is:

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A⁶
1. A solution comprising an N-terminal domain of TNFR-1 associated death domain protein (N-TRADD).
 2. The solution of Claim 1, wherein the N-terminal domain of TNFR-1 associated death domain protein comprises amino acid residues 1-169 of Figure 1.
 3. The solution of Claim 2, comprising between 0.8-1.0 mM N-TRADD in a buffer comprising 20mM imidazole, 200 mM NaCl, 20 mM DTT and 0.05% NaN₃, in either 90% H₂O/10% D₂O or 100% D₂O.
 4. The solution of Claim 3, wherein the N-TRADD is either unlabeled, ¹⁵N enriched or ¹⁵N, ¹³C enriched.
 5. The solution of Claim 4, wherein the N-TRADD is biologically active.
 6. The solution of Claim 1, wherein the secondary structure of N-TRADD comprises four beta strands forming an antiparallel beta sheet, with five alpha helices packing around the beta sheet.
 7. The solution of Claim 6, wherein the beta strands and alpha helices are configured in the trace order $\beta 1$, $\alpha 1$, $\alpha 2$, $\beta 2$, $\beta 3$, $\alpha 3$, $\beta 4$, $\alpha 4$ and $\alpha 5$.
 8. The solution of Claim 7, wherein $\beta 1$ comprises amino acid residues S14-E20 of N-TRADD, $\alpha 1$ comprises amino acid residues L28-Y32 of N-TRADD, $\alpha 2$ comprises amino acid residues P35-G53 of N-TRADD, $\beta 2$ comprises amino acid residues Q60-R66 of N-TRADD, $\beta 3$ comprises amino acid residues L71-R76 of N-TRADD, $\alpha 3$ comprises amino acid residues R80-L107 of N-TRADD, $\beta 4$ comprises

amino acid residues Q115-R119 of N-TRADD, α 4 comprises amino acid residues E132-A141 of N-TRADD and α 5 comprises amino acid residues E150-N161 of N-TRADD.

9. An active site of a C-TRAF2 binding protein or peptide, wherein said active site is characterized by a three dimensional structure comprising the relative structural coordinates of amino acid residues Y16, F18, and H65 according to Figure 2, \pm a root mean square deviation from the conserved backbone atoms of said amino acids of not more than 1.5 Å.

10. The active site of Claim 9, wherein the three dimensional structure of said active site further comprises the relative structural coordinates of amino acid residues L17, V58, L59, I72, and D149 according to Figure 2, \pm a root mean square deviation from the conserved backbone atoms of said amino acids of not more than 1.5 Å.

11. The active site of Claim 10, wherein the three dimensional structure of said active site further comprises the relative structural coordinates of amino acid residues K63, I64, D68, Q70, V73, Q74, L75, C78, L118, G121, A122, R124, L125, E150, and L152 according to Figure 2, \pm a root mean square deviation from the conserved backbone atoms of said amino acids of not more than 1.5 Å.

12. The active site of Claim 10, wherein the root mean square deviation from the conserved backbone atoms of said amino acids is not more than 1.0 Å.

13. The active site of Claim 10, wherein the root mean square deviation from the conserved backbone atoms of said amino acids is not more than 0.5 Å.

14. An agent which binds to the active site of Claim 9, wherein said agent is an inhibitor of TRADD function.

15. The agent of Claim 14, wherein said agent is a protein, peptide, nucleic acid or compound.

16. An agent which binds to the active site of Claim 10, wherein said agent is an inhibitor of TRADD function.

17. The agent of Claim 16, wherein said agent is a protein, peptide, nucleic acid or compound.

18. An agent which binds to the active site of Claim 11, wherein said agent is an inhibitor of TRADD function.

19. The agent of Claim 18, wherein said agent is a protein, peptide, nucleic acid or compound.

20. A method for identifying an agent that interacts with N-TRADD, comprising the steps of:

- (a) determining an active site of N-TRADD from a three dimensional structure of N-TRADD; and
- (b) performing computer fitting analyses to identify an agent which interacts with said active site.

21. The method of Claim 20, wherein the active site comprises the relative structural coordinates of amino acid residues Y16, F18, and H65 according

to Figure 2, \pm a root mean square deviation from the conserved backbone atoms of said amino acids of not more than 1.5 Å.

22. The method of Claim 21, wherein the active site further comprises the relative structural coordinates of amino acid residues L17, V58, L59, I72, and D149 according to Figure 2, \pm a root mean square deviation from the conserved backbone atoms of said amino acids of not more than 1.5 Å.

23. The method of Claim 22, wherein the active site further comprises the relative structural coordinates of amino acid residues K63, I64, D68, Q70, V73, Q74, L75, C78, L118, G121, A122, R124, L125, E150, and L152 according to Figure 2, \pm a root mean square deviation from the conserved backbone atoms of said amino acids of not more than 1.5 Å.

24. The method of Claim 21, further comprising contacting the identified agent with a molecule or molecular complex comprising N-TRADD in order to determine the effect the agent has on said molecule or molecular complex.

25. The method of Claim 24, wherein the agent is an inhibitor of the molecule or molecular complex comprising N-TRADD.

26. An agent identified by the method of Claim 25.

27. A method for identifying an agent which is a potential inhibitor of N-TRADD binding to C-TRAF2, comprising the steps of:

- (a) determining an N-TRADD binding active site of C-TRAF2 from a three dimensional structure of N-TRADD and a three dimensional structure of C-TRAF2;

- (b) selecting or designing a candidate inhibitor of N-TRADD binding to C-TRAF2 by performing computer fitting analyses with the three dimensional structures of (a); and
- (c) obtaining or synthesizing the candidate inhibitor.

28. The method of Claim 27, comprising the additional step of contacting the candidate inhibitor with N-TRADD and C-TRAF2 in solution in order to determine the effect of the candidate inhibitor on N-TRADD binding to C-TRAF2.

29. The method of Claim 27, wherein the N-TRADD binding active site of C-TRAF2 comprises the relative structural coordinates of amino acid residues R393, Y395, D399, G400, F410, F447, R448, P449, D450, S453, S454, S455, I465, A466, S467, G468, and P470 according to the atomic coordinates specified in Accession Nos. 1CA4, 1CA9 or 1QSC of the Protein Data Bank, \pm a root mean square deviation from the conserved backbone atoms of said amino acids of not more than 1.5 Å.

30. A method for identifying a potential inhibitor of N-TRADD, comprising the steps of:

- (a) using a three dimensional structure of N-TRADD as defined by the relative structural coordinates of the amino acids of Figure 2, \pm a root mean square deviation from the conserved backbone atoms of said amino acids of not more than 1.5 Å;
- (b) employing said three-dimensional structure to design or select a potential inhibitor; and
- (c) synthesizing or obtaining said potential inhibitor.

31. The method according to Claim 30, wherein the potential inhibitor is designed *de novo*.

32. The method according to Claim 30, wherein the potential inhibitor is designed from a known inhibitor.

33. The method of Claim 31, further comprising the step of contacting the potential inhibitor with N-TRADD in the presence of a binding protein to determine the ability of the potential inhibitor to inhibit N-TRADD.

34. The method of Claim 32, further comprising the step of contacting the potential inhibitor with N-TRADD in the presence of a binding protein to determine the ability of the potential inhibitor to inhibit N-TRADD.

35. The method according to Claim 30, wherein the step of employing the three dimensional structure to design or select the potential inhibitor comprises the steps of:

- (a) identifying chemical entities or fragments capable of associating with N-TRADD; and
- (b) assembling the identified chemical entities or fragments into a single molecule to provide the structure of the potential inhibitor.

36. The method according to Claim 35, wherein the potential inhibitor is designed *de novo*.

37. The method according to Claim 35, wherein the potential inhibitor is designed from a known inhibitor.

38. The method of Claim 36, further comprising the step of contacting the potential inhibitor with N-TRADD in the presence of a binding protein to determine the ability of the potential inhibitor to inhibit N-TRADD.

39. The method of Claim 37, further comprising the step of contacting the potential inhibitor with N-TRADD in the presence of a binding protein to determine the ability of the potential inhibitor to inhibit N-TRADD.

40. An inhibitor identified or designed by the method of Claim 31.

41. An inhibitor identified or designed by the method of Claim 35.